## REMARKS

This Request for Continued Examination and Response is being filed in connection with the Final Office Action mailed October 21, 2005. Claims 8 to 11, 20 to 28, 30 and 31 are pending. Claims 22 to 28 and 30 stand withdrawn from consideration as directed to a non-elected invention. By this Response, claim 31 has been canceled herein without prejudice. Applicants maintain the right to prosecute the canceled claim in any related application claiming the benefit of priority of the subject application. Accordingly, upon entry of the amendment, claims 8 to 11, 20 and 21 are under consideration.

*Regarding the Claim Amendments*

Support for the amendments to claims 8 to 11, 20 and 21 can be found throughout the specification. In particular, the amendment to recite "anti-CD40 antibody" is supported, for example, at page 6, lines 12-23; page 8, lines 5-19; page 15, lines 10-12; page 15, lines 26-27; and at page 22, lines 20-27. The amendment to claims 8 to 11 to recite "in the presence of a mixture of human flag-tagged CD40L at 1 ug/ml and CD40L enhancer antibody at 1 ug/ml" is supported, for example, at page 69, lines 10-14. The amendment to claims 8 to 11 deleting the recitation of "CD40L (1 μg/ml) mediated" was made in order to eliminate redundant language and, therefore, was made to address an informality. Thus, as the claim amendments are supported by the specification or were made to address an informality, no new matter has been added and entry thereof is respectfully requested.

I. REJECTIONS UNDER 35 U.S.C. §112

The rejection of claim 31 under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement is respectfully traversed. Allegedly, "it would have been undue experimentation to make and use the vast repertoire of amino acids to enable the scope of the functional anti-CD40 antibodies encompassed."

Claim 31 is adequately enabled. In this regard, the specification teaches the skilled artisan how to make and use the claimed antibodies, including modified forms, without undue experimentation. For example, the specification discloses various methods of producing anti-

CD40 antibodies and modified forms (see, for example, page 23, line 14, to page 25, line 23; page 27, line 6, to page 30, line 6; page 55, line 19, to page 57, line 13; and page 59, line 17, to page 63, line 11). The specification also discloses assays for identifying anti-CD40 antibodies having the requisite activity (see, for example, page 57, line 18, to page 58, line 5; page 64, line 24, to page 65, line 14; and page 69, lines 6-17). In view of the guidance in the specification, the skilled artisan could readily produce the antibodies of claim 31. With respect to using the antibodies of claim 31, the specification teaches a variety of methods of using such antibodies without undue experimentation including, for example, among other things modulating CD40 activity (see, e.g., page 36, line 19, to page 38, line 14), and detecting or purifying or monitoring CD40 (see, e.g., page 50, line 11, to page 52, line 22). Thus, in view of the guidance in the specification, the skilled artisan could make and use the antibodies of claim 31 without undue experimentation.

Nevertheless, solely in order to further prosecution of the application and without acquiescing to the propriety of the rejection, claim 31 has been canceled herein without prejudice. Accordingly, the rejection under 35 U.S.C. §112, first paragraph, is moot.

II. REJECTIONS UNDER 35 U.S.C. §102

*U.S. Patent No. 5,874,082 (De Boer)*

The rejection of claims 8 to 11, 20, 21 and 31, under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent No. 5,874,082 (De Boer) is respectfully traversed. Allegedly, de Boer describe the claimed antagonistic anti-CD40 antibodies.

Claim 31 has been canceled herein without prejudice. Accordingly, the rejection of claim 31 is moot.

As to claims 8 to 11, 20 and 21, these claims have been amended to more clearly indicate the conditions used to ascertain the extent to which the claimed anti-CD40 antibodies reduce tonsillar B-cell proliferation in vitro. In particular, the amended claims recite "in the presence of a mixture of human flag-tagged CD40L at 1 ug/ml and CD40L enhancer antibody at 1 ug/ml."

deBoer fail to teach or suggest the claimed anti-CD40 antibodies because 1) the claims require that the anti-CD40 antibodies have the ability to inhibit CD40L mediated tonsillar B cell proliferation in vitro to a particular extent, whereas the 5D12 antibody mentioned in deBoer fails to have the ability to inhibit CD40L mediated tonsillar B cell proliferation in vitro to this extent under the same assay conditions recited in the claims; and 2) the 3C6, 3A8, humanized Fab and chimeric 5D12 antibodies reported in deBoer all have essentially the same tonsillar B cell proliferation inhibitory efficiency as 5D12. Accordingly, because none of the antibodies mentioned in deBoer have the ability to inhibit CD40L mediated tonsillar B cell proliferation in vitro to the extent required by claims 8 to 11, 20 and 21, deBoer fails to anticipate claims 8 to 11, 20 and 21.

With respect to inhibition of CD40L mediated tonsillar B cell proliferation in vitro, the specification discloses tonsillar B cell proliferation studies directly comparing antibody 5D12 to particular examples of the claimed antibodies, namely F4-465 and No. 72 (Example 6, page 68 to page 70). The results of these studies are illustrated in Figure 10. In brief, these studies indicate that under identical assay conditions that 5D12 inhibited CD40L mediated tonsillar B cell proliferation in vitro but not nearly to the extent of F4-465 and No. 72 antibodies (page 69, line 21, to page 70, line 8). In particular, for example, both F4-465 and No. 72 antibodies inhibited B cell proliferation to almost 95% at concentrations of 1-10 ug/ml. In contrast, under identical assay conditions, 5D12 only achieved a maximum of 50% inhibition at concentrations requiring at least 10-fold more antibody (i.e., 100 ug/ml). Accordingly, in view of the foregoing studies performed under identical assay conditions, it is clear that 5D12 does not have the ability to inhibit CD40L mediated tonsillar B cell proliferation in vitro to the extent required in claims 8 to 11, 20 and 21, namely about 50 to 95% or greater reduction, about a 85 to 95% or greater reduction, about 80 to 95% or greater reduction, or about a 95% or greater reduction, at the amount required, namely 0.01 ug/ml to 10 ug/ml, 0.1 ug/ml to 10 ug/ml, 0.01 ug/ml to 10 ug/ml, and 0.1 ug/ml to 10 ug/ml, respectively.

With respect to the other antagonist antibodies in deBoer, the data in deBoer indicate that 5D12, 3A8 and 3C6 all have virtually the same tonsillar B cell proliferation inhibitory efficiency (see, Figures 6 and 7). deBoer describe humanized 5D12 Fab and a chimeric 5D12, each of

which were also shown to have the same competitive binding characteristics relative to the parent antibody 5D12 (see, column 32, lines 7-14). Thus, the data in deBoer indicate that all of the anti-CD40 antibodies described by deBoer, namely 3A8, 3C6, humanized 5D12 Fab and chimeric 5D12, essentially have the same tonsillar B cell proliferation inhibiting efficiency as 5D12.

As discussed above, the specification discloses studies of 5D12 under the assay conditions recited in claims 8 to 11, 20 and 21. The studies disclosed in the specification clearly indicate that 5D12 does not have the ability to inhibit CD40L mediated tonsillar B cell proliferation in vitro as is required for the antibodies of claims 8 to 11, 20 and 21. The studies comparing 5D12 to examples of the claimed antibodies, namely F4-465 and No. 72, were under identical conditions, further indicating that the data obtained was not a result of the assay conditions. Accordingly, in view of the fact that 5D12 does not have the ability to inhibit CD40L mediated tonsillar B cell proliferation in vitro required of the claimed antibodies, and the data in deBoer indicate that A8, 3C6, humanized 5D12 Fab and chimeric 5D12, all essentially have the same tonsillar B cell proliferation inhibiting efficiency as 5D12, it is clear that none of the antibodies in deBoer have the ability to inhibit CD40L mediated tonsillar B cell proliferation in vitro as required for the antibodies of claims 8 to 11, 20 and 21.

It is noted that the deBoer B-cell proliferation assay used ELB45 cells to induce proliferation in vitro (see column 11, line 55, to column 12, line 4; and example 5, column 18, line 46, to column 19, line 25), whereas the assay conditions disclosed in the specification and recited in the claims use CD40L as the inducer of B-cell proliferation. This difference, among others, may explain why deBoer reported that 5D12, A8 and 3C6, appeared to exhibit "potent inhibition" of B-cell proliferation (column 19, lines 3-6). However, as discussed above, in view of the direct comparison studies with 5D12 disclosed in the specification, it is clear that the antibodies in deBoer do not have the ability to inhibit CD40L mediated tonsillar B cell proliferation required of the claimed antibodies.

In sum, deBoer fails to teach or suggest anti-CD40 antibodies and fragments thereof having the requisite ability to inhibit CD40L mediated tonsillar B cell proliferation in vitro, as

required in claims 8 to 11, 20 and 21. Accordingly, as deBoer fail to teach or suggest each and every element of claims 8 to 11, 20 and 21, the claims are not anticipated by deBoer and Applicants respectfully request that the rejection under 35 U.S.C. §102(e) be withdrawn.

*U.S. Patent Application Publication 2004/0235074 A1 (Siegall et al.)*

The rejection of claims 8 to 11, 20, 21 and 31, under 35 U.S.C. §102(e) as allegedly anticipated by U.S. Patent Application Publication 2004/0235074 A1 (Siegall *et al.*) is respectfully traversed. Allegedly, Siegall *et al.* describe the claimed antagonistic anti-CD40 antibodies.

Claim 31 has been canceled herein without prejudice. Accordingly, the rejection of claim 31 is moot.

As to claims 8 to 11, 20 and 21, as discussed above, the claims have been amended to more clearly indicate the assay conditions used to ascertain the extent to which the claimed anti-CD40 antibodies reduce tonsillar B-cell proliferation in vitro. In this regard, Siegall *et al.* fail to teach or suggest the claimed anti-CD40 antibodies that inhibit CD40L mediated tonsillar B cell proliferation in vitro at the recited inhibitory efficiencies. Siegall *et al.* describe the same antagonist anti-CD40 antibodies as deBoer, namely 5D12, 3A8 and 3C6. As discussed above, in direct comparison studies, 5D12 antibody did not have the requisite ability to inhibit CD40L mediated tonsillar B cell proliferation in vitro as required for the antibodies of claims 8 to 11, 20 and 21. As also discussed above, the data in deBoer indicate that the anti-CD40 antibodies 3A8, 3C6 have the same tonsillar B cell proliferation inhibiting efficiency as 5D12. Consequently, none of the antibodies in Siegall *et al.* have the ability to inhibit CD40L mediated tonsillar B cell proliferation in vitro as required for the antibodies of claims 8 to 11, 20 and 21.

In sum, Siegall *et al.* fails to teach or suggest anti-CD40 antibodies or fragments thereof having the requisite to inhibit CD40L mediated tonsillar B cell proliferation in vitro, as required of claims 8 to 11, 20 and 21. Accordingly, as Siegall *et al.* fail to teach or suggest each and every element of claims 8 to 11, 20 and 21, the claims are not anticipated by Siegall *et al.* and Applicants respectfully request that the rejection under 35 U.S.C. §102(e) be withdrawn.

III. OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTION

The provisional rejection of claims 8 to 11, 20, 21 and 31, under the judicially created doctrine of obviousness-type double patenting over claims 3, 6, 8, 23 to 26 and 65 to 71 of application serial no. 09/844,684, is respectfully traversed.

Claim 31 has been canceled herein without prejudice. Accordingly, the rejection of claim 31 is moot.

Applicants respectfully request that this rejection be held in abeyance until such time as allowable subject matter has been indicated. Applicants will file an appropriate response upon the indication of allowable subject matter.

## CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 8 to 11, 20 and 21 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 509-4065.

Please charge any fees associated with the submission of this paper to Deposit Account Number 033975. The Commissioner for Patents is also authorized to credit any over payments to the above-referenced Deposit Account.

Respectfully submitted,

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